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L3           595 SEA FILE=REGISTRY SSS FUL L2
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L4              STR
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                ACT SPI118SUB1/A
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L5              STR
L6   (       595)SEA FILE=REGISTRY SSS FUL L5
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L8           412 SEA FILE=REGISTRY SUB=L6 SSS FUL L7
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L10           52 S SHIBOUTA Y?/AU
L11         2993 S KUBO K?/AU
L12         5686 S L9-L11
L13           15 S L12 AND GLOMERULONEPHRITIS

     FILE 'REGISTRY' ENTERED AT 11:00:46 ON 08 JUL 2005
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L16 370 S L14 FUL SUB=L8

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L17 15 S L16 AND GLOMERULONEPHRITIS
SELECT L13 RN 1-15
SELECT L17 RN 1-15
SAVE TEMP SPI118CHI2/Q L14

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FILE 'HCAPLUS' ENTERED AT 12:47:19 ON 08 JUL 2005

FILE 'HCAPLUS' ENTERED AT 12:47:52 ON 08 JUL 2005

=> d l13 ibib abs 1-15

L13 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:182765 HCAPLUS
DOCUMENT NUMBER: 137:245322
TITLE: Significance of urinary wt1 mRNA detection and isoforms analysis in progressive nephropathy
AUTHOR(S): **Kubo, Kanae**; Mimura, Toshihide
CORPORATE SOURCE: Graduate School of Medicine, Tokyo University, Japan
SOURCE: Annual Review Jinzo (2002) 46-49
CODEN: ARJNB2
PUBLISHER: Chugai Igakusha
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review on Wilms' tumor suppressor WT1 mRNA and its isoforms in patients with nephropathy. The topics discussed are (1) transcription factor WT1 and alternative splicing of the Wilms' tumor suppressor gene wt1; (2) detection of wt1 mRNA in urine; (3) urinary wt1 mRNA as a marker of progressive nephropathy; and (4) urinary wt1 mRNA isoforms in patients with progressive nephropathy.

L13 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:635351 HCAPLUS
DOCUMENT NUMBER: 136:334964
TITLE: Effects of a new synthetic selectin blocker in an acute rat thrombotic **glomerulonephritis**
AUTHOR(S): Ito, Isao; Yuzawa, Yukio; Mizuno, Masashi; **Nishikawa, Kazuhiro**; Tashita, Akira; Jomori, Takahito; Hotta, Nigishi; Matsuo, Seiichi
CORPORATE SOURCE: Third Department of Internal Medicine, Nagoya University School of Medicine, Aichi, 466-8550, Japan
SOURCE: American Journal of Kidney Diseases (2001), 38(2), 265-273
CODEN: AJKDDP; ISSN: 0272-6386
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In an attempt to explore a novel therapeutic approach, a new synthetic sulfatide derivative (SKK60037) was evaluated in an acute rat model of P-selectin and leukocyte-dependent thrombotic **glomerulonephritis** (TG). In vitro, SKK60037 inhibits the function of P- and L-selectin more effectively than sialyl Lewis X (sLex), a well-established selectin blocker. TG was induced by the i.v. administration of nephrotoxic globulin (NTG) to rats pretreated with a subclin. dose of

lipopolysaccharide. In this model, platelet accumulation was remarkable within 10 min after induction of disease, followed by the infiltration of leukocytes, mainly neutrophils and macrophages. Thrombus formation and fibrinogen deposition in the glomeruli were observed within 1 h, and they proceeded until 6 h. P-selectin was highly expressed in glomeruli, whereas E-selectin and L-selectin ligands were not detected. We tested the effects of SKK60037 in this model in comparison with sLex and anti-rat P-selectin monoclonal antibody (ARP2-4). SKK60037 blocked platelet accumulation in glomerular capillaries at 10 min after NTG injection. At 6 h, leukocyte infiltration and thrombosis were significantly suppressed. Protective effects of SKK60037 were similar to those of ARP2-4, whereas sLex showed min. effect. The superior effects and more favorable characteristics of SKK60037 to sLex suggest the potential of SKK60037 for clin. application.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:513558 HCAPLUS
DOCUMENT NUMBER: 136:182316
TITLE: The role of C5a in the development of thrombotic **glomerulonephritis** in rats
AUTHOR(S): Kondo, C.; Mizuno, M.; **Nishikawa, K.**; Yuzawa, Y.; Hotta, N.; Matsuo, S.
CORPORATE SOURCE: The Third Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, 466-8550, Japan
SOURCE: Clinical and Experimental Immunology (2001), 124(2), 323-329
CODEN: CEXIAL; ISSN: 0009-9104
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Thrombus formation is the important pathol. finding observed in **glomerulonephritis** induced by antiglomerular basement membrane (GBM) antibodies. Although strong deposition of C3 and membrane attack complex (MAC) is observed in this disease, the role of complement has not been fully elucidated. The aim of this work was to investigate the role of complement, especially an anaphylatoxin C5a, in a rat model of thrombotic **glomerulonephritis**. Rats were first pretreated with subclin. dose of lipopolysaccharide (LPS). Thrombotic **glomerulonephritis** was then induced by i.v. injection with rabbit anti-rat GBM (RbAGBM) (Group I). For the evaluation of the role of complement, the soluble complement receptor type 1 (sCR1) (Group II) or the C5a receptor antagonist peptide (C5aR-AP) (Group III) was i.v. administered 30 min before RbAGBM injection. For exploring the role of neutrophils, rats were pretreated with cyclophosphamide before induction of disease (Group IV). All rats were sacrificed at 6 h, and histol. examination was performed. Rats in Group I developed severe glomerular thrombosis. Leukocyte accumulation and strong binding of C3 and MAC were observed in the glomeruli. In rats treated with sCR1 (Group II) and C5aR-AP (Group III), both leukocyte accumulation and thrombus formation in the glomeruli were significantly inhibited. C3 and MAC were neg. in the glomeruli in Group II rats, while they were strongly observed in Group III. In neutrophil depleted rats (Group IV), there was also deposition of C3 and MAC in the glomeruli but thrombus formation was not observed These findings indicated that glomerular thrombosis is dependent on the leukocytes, and mediated in part by the anaphylatoxin C5a but not MAC in the present model.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:717202 HCAPLUS
DOCUMENT NUMBER: 133:15799
TITLE: Detection of WT1 mRNA in urine from patients with kidney diseases
AUTHOR(S): **Kubo, K.**; Miyagawa, K.; Yamamoto, R.; Hamasaki, K.; Kanda, H.; Fujita, T.; Yamamoto, K.; Yazaki, Y.; Mimura, T.
CORPORATE SOURCE: Department of Internal Medicine, University of Tokyo, Tokyo, 113-8655, Japan
SOURCE: European Journal of Clinical Investigation (1999), 29(10), 824-826
CODEN: EJCIB8; ISSN: 0014-2972
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Detachment of glomerular epithelial cells (GEC) from glomerular basement membrane (GBM) could account for a part of the pathogenic mechanism of proteinuria seen in primary and secondary renal diseases. The Wilms' tumor suppressor gene (WT1) is strictly expressed in GEC in the adult kidney. Mutations of WT1 gene have been implicated in progressive renal damage. Utilizing nested RT-PCR we detected mRNA of WT1 in the urine of patients with renal diseases. Seven of 20 (35%) chronic **glomerulonephritis** (CGN), eight of 20 (40%) diabetes mellitus (DM) with proteinuria, and two of 24 (8.3%) rheumatic diseases were WT1 pos. Interestingly, only one of 51 (2%) DM without proteinuria was WT1 pos. None of the healthy volunteers or cystitis patients were WT1 pos. This is the first report describing the detection of endogenous WT1 mRNA, an important gene in progressive renal failure, from patients' urine. This technique could be a powerful tool in the search for information about glomerular damage in clin. settings as well as for WT1 mutations or isoform imbalance at the research level without renal biopsy.
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:138681 HCAPLUS
DOCUMENT NUMBER: 131:3885
TITLE: Immunomodulation of the CD28-B7 system: effects of inhibition of co-stimulatory signals provided by CD28-B7 interaction on rat autoimmune anti-glomerular basement membrane **glomerulonephritis**
AUTHOR(S): **Nishikawa, K.**; Matsuo, S.
CORPORATE SOURCE: Division of Nephrology, The Third Department of Internal Medicine, Nagoya University School of Medicine, Nagoya, 466-8550, Japan
SOURCE: Nephrology, Dialysis, Transplantation (1999), 14(Suppl. 1), 19-21
CODEN: NDTREA; ISSN: 0931-0509
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review and discussion with 8 refs. of the title subject and some new material from the authors' laboratory In those expts. rats injected with CTLA-4Ig from the time of immunization had decreased levels of circulating antibody to the α3 chain of type IV collagen, reduced intensity of deposition of rat IgG in the glomerular basement membrane as well as reduced disease severity. Beneficial effects were observed even when injections were started after the onset of **glomerulonephritis**. The results provide evidence for CD28 signaling in rat autoimmune

glomerulonephritis.
REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:704823 HCAPLUS
DOCUMENT NUMBER: 130:75996
TITLE: Beneficial effects of a novel inhibitor of platelet-derived growth factor receptor autophosphorylation in the rat with mesangial proliferative **glomerulonephritis**
AUTHOR(S): Yagi, Mikio; Kato, Shinichiro; Kobayashi, Yoshiko; Kobayashi, Nami; Iinuma, Noriko; Nakamura, Kazuhide; **Kubo, Kazuo**; Ohyama, Shin-Ichi; Murooka, Hideko; Shimizu, Toshiyuki; Nishitoba, Tsuyoshi; Osawa, Tatsushi; Nagano, Nobuo
CORPORATE SOURCE: PHARMACEUTICAL RESEARCH LABORATORY, KIRIN BREWERY CO., LTD., TAKASAKI, 370-1295, Japan
SOURCE: General Pharmacology (1998), 31(5), 765-773
CODEN: GEPHDP; ISSN: 0306-3623
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 1. Our original compound, Ki6896 ((4-t-butylphenyl){4-[(6,7-dimethoxy-4-quinolyl)oxy]phenyl}methanone) strongly inhibited the autophosphorylation of platelet-derived growth factor (PDGF) β-receptor (IC50=0.31 μM) and that of basic fibroblast growth factor receptor (IC50=3.1 μM), whereas it did not inhibit some other kinases. 2. The [3H]thymidine incorporation and the growth of mesangial cells under the stimulation of PDGF were inhibited by Ki6896 in a dose-dependent manner. 3. In the mesangial proliferative **glomerulonephritis** rats induced by anti-Thy-1 monoclonal antibody, glomerulosclerosis was ameliorated and the number of glomerular proliferating cells was decreased by the daily administration of Ki6896. However, the accumulation of type I collagen and fibronectin in the glomeruli was not suppressed by Ki6896.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:639578 HCAPLUS
DOCUMENT NUMBER: 127:306517
TITLE: The role of complement in the pathogenesis of tubulointerstitial lesions in rat mesangial proliferative **glomerulonephritis**
AUTHOR(S): Morita, Yoshiki; Nomura, Atsushi; Yuzawa, Yukio; **Nishikawa, Kazuhiro**; Hotta, Nigishi; Shimizu, Fujio; Matsuo, Seiichi
CORPORATE SOURCE: The Third Department of Internal Medicine, Nagoya University School of Medicine, Tsuruma, 466, Japan
SOURCE: Journal of the American Society of Nephrology (1997), 8(9), 1363-1372
CODEN: JASNEU; ISSN: 1046-6673
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Persistent proteinuria and tubulointerstitial lesions are important signs of progressive renal disease. The purpose of this study was to assess the role of complement in the development of tubulointerstitial lesions in rats with proteinuria due to primary **glomerulonephritis**. Mesangial proliferative **glomerulonephritis** was induced in

mono-nephrectomized rats by i.v. injection of monoclonal antibody (mAb) 1-22-3. As early as 24 h after the injection, proteinuria became evident, persisted throughout the observation period, and was associated with mesangial cell proliferation and tubulointerstitial lesions when examined at 7 and 14 d after mAb administration. Deposition of rat C3 and C5b-9 was observed at the luminal surface of proximal tubules and in cellular debris present in the tubular lumen (group I). Rats injected with mAb 1-22-3 and depleted of complement by injections of cobra venom factor starting at day 3 developed **glomerulonephritis** and proteinuria comparable to rats of group I, but complement deposition in the tubules and the tubulointerstitial lesions were markedly reduced (group II). Rats in group III were injected with mAb and, from day 3, with soluble complement receptor type 1, which became detectable at the luminal surface of proximal tubules and in the urine. Deposition of C5b-9 in tubular cells was not detectable, and the severity of tubulointerstitial lesions was reduced compared with rats in group I. These results indicate that, in this model of primary mesangial proliferative **glomerulonephritis** with proteinuria, the development of tubulointerstitial lesions is associated with activation of serum complement at the level of tubular brush border, and tubulointerstitial lesions can be reduced by inhibition of complement activity.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:971367 HCAPLUS
DOCUMENT NUMBER: 124:115173
TITLE: Embryonic fibronectin isoforms are synthesized in crescents in experimental autoimmune **glomerulonephritis**
AUTHOR(S): Nickeleit, Volker; Zagachin, Luba; **Nishikawa, Kazuhiro**; Peters, John H.; Hynes, Richard O.; Colvin, Robert B.
CORPORATE SOURCE: Harvard Medical School, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: American Journal of Pathology (1995), 147(4), 965-78
CODEN: AJPAA4; ISSN: 0002-9440
PUBLISHER: American Society for Investigative Pathology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Crescents are a severe and stereotyped glomerular response to injury that occur in several forms of **glomerulonephritis** that progress to renal failure. The key pathogenic step that leads to glomerular scarring is unknown, but fibronectin (FN), the clotting system, macrophages, and proliferating parietal epithelial cells are known to participate. This study was designed to determine whether FN is synthesized locally, and in what mol. isoform, and whether cytokines known to promote FN synthesis are present in the crescent. Rats immunized with bovine glomerular basement membrane develop cellular crescents by 14 days and fibrous crescents and glomerulosclerosis by 35 days. In situ hybridization was performed with oligonucleotides specific for sequences common to all FN isoforms (total FN) or sequences specific for the alternatively spliced segments (EIIIA, EIIIB, and V). Throughout the time period (14, 21, and 35 days) all crescents and glomerular tufts contained cells with strong in situ hybridization (ISH) signals for total and V+ mRNA, with the strongest signals present in large cellular crescents at day 21. In contrast, EIIIA+ and EIIIB+ mRNAs showed maximal abundance within sclerosing crescents at 35 days. Protein deposition of EIIIA+, EIIIB+, and V+ FN isoforms was confirmed by immunofluorescence with segment-specific FN antibodies. Transforming growth factor-β and interleukin-1 β,

both known to promote FN synthesis, were found in cellular crescents (days 14 and 21) and were still present, but greatly diminished, in the sclerotic phase (day 35). Thus, EIIIA-, EIIIB-, and V+ FN mRNA plasma isoforms predominate in cellular crescents, whereas in the fibrosing stage, mainly the oncofetal EIIIA+, EIIIB+, and V+ isoforms are synthesized and accumulate.

L13 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:336317 HCAPLUS
DOCUMENT NUMBER: 122:102738
TITLE: Glomerular basement membrane and **glomerulonephritis**
AUTHOR(S): Matsuo, Seiichi; **Nishikawa, Kazuhiro**
CORPORATE SOURCE: Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SOURCE: Igaku no Ayumi (1994), 171(6), 530-4
CODEN: IGAYAY; ISSN: 0039-2359
PUBLISHER: Ishiyaku
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review of the structure and the function of glomerular basement membrane and the relation to **glomerulonephritis** with 7 refs. The etiol. and the pathol. of Goodpasture's syndrome and Alport's syndrome, and also the animal model of glomerular basement membrane **glomerulonephritis** were described.

L13 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:708347 HCAPLUS
DOCUMENT NUMBER: 121:308347
TITLE: Pharmaceutical compositions containing angiotensin II antagonists for prevention and treatment of diabetic nephropathy or **glomerulonephritis**
INVENTOR(S): **Nishikawa, Kohei; Shibouta, Yumiko ; Kubo, Keiji**
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 622077	A1	19941102	EP 1994-106203	19940421
EP 622077	B1	20000705		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 07002667	A2	19950106	JP 1994-81705	19940420
JP 2003306432	A2	20031028	JP 2003-149577	19940420
CA 2121871	AA	19941023	CA 1994-2121871	19940421
AT 194284	E	20000715	AT 1994-106203	19940421
PT 622077	T	20001031	PT 1994-106203	19940421
ES 2149226	T3	20001101	ES 1994-106203	19940421
AU 677702	B2	19970501	AU 1994-75815	19941013
AU 9475815	A1	19960426		
US 5719173	A	19980217	US 1996-696475	19960814
US 5889036	A	19990330	US 1997-965416	19971106
US 6040324	A	20000321	US 1998-207043	19981208
US 6319938	B1	20011120	US 1999-467488	19991220
GR 3033862	T3	20001031	GR 2000-401469	20000706
US 2002045652	A1	20020418	US 2001-977476	20011016

US 6469037	B2	20021022		
US 2003114509	A1	20030619	US 2002-227537	20020826
US 6686383	B2	20040203		
US 2004082636	A1	20040429	US 2003-676118	20031002

PRIORITY APPLN. INFO.:

JP 1993-95942	A 19930422
US 1994-229930	A3 19940419
JP 1994-81705	A3 19940420
US 1996-696475	A3 19960814
US 1997-965416	A1 19971106
US 1998-207043	A3 19981208
US 1999-467488	A3 19991220
US 2001-977476	A3 20011016
US 2002-227537	A3 20020826

OTHER SOURCE(S): MARPAT 121:308347

AB Pharmaceutical compns. containing angiotensin II antagonists are useful for prevention and treatment of diabetic nephropathy or **glomerulonephritis**. Rats who had undergone nephrectomy of 2/3 of left kidney and whole right kidney were orally administered 1mg/kg/day of (±)-1-(cyclohexyloxycarbonyloxy)ethyl-2-ethoxy-1-[[2'-(1H-tetrazole-5-yl)biphenyl-4-yl]methyl]-1H-benzimidazole-7-carboxylate (I) once a day for 8 wk. The total urinary protein after 8 wk was 24.4 as compared with 55.1 mg/100g/24 h for controls.

L13 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:506058 HCAPLUS
DOCUMENT NUMBER: 121:106058
TITLE: The role of adhesion molecules in **glomerulonephritis**
AUTHOR(S): **Nishikawa, Kazuhiro**; Matsuo, Seiichi
CORPORATE SOURCE: Sch. Med., Nagoya Univ., Nagoya, 466, Japan
SOURCE: Saishin Igaku (1994), 49(6), 1199-204
CODEN: SAIGAK; ISSN: 0370-8241
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review, with 12 refs., on antiinflammatory effect of various anti-adhesion mol. antibodies on Masugi nephritis and anti-ICAM-1 antibody and anti-LFA-1 antibody on exptl. autoimmune **glomerulonephritis**, and inhibition of costimulatory signal by CTLA-4 (CD28)-IgG fusion protein for treatment of autoimmune nephritis.

L13 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:433016 HCAPLUS
DOCUMENT NUMBER: 121:33016
TITLE: Effect of CTLA-4 chimeric protein on rat autoimmune anti-glomerular basement membrane **glomerulonephritis**
AUTHOR(S): **Nishikawa, Kazuhiro**; Linsley, Peter S.; Collins, A. Bernard; Stamenkovic, Ivan; McCluskey, Robert T.; Andres, Giuseppe
CORPORATE SOURCE: Dep. Pathol., Massachusetts Gen. Hosp., Boston, MA, USA
SOURCE: European Journal of Immunology (1994), 24(6), 1249-54
CODEN: EJIMAF; ISSN: 0014-2980
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interaction of the T cell receptor with the antigen/major histocompatibility class II complex is insufficient to induce optimal T cell activation. Co-stimulatory signals, including those provided by CD28/CTLA-4 on T cells and B7 mols. (B7-1, -2, and -3) on antigen-presenting cells, are also required. CD28-B7 interactions can be

blocked by a soluble human CTLA-4 chimeric protein (CTLA4Ig). The authors tested the effect of administration of CTLA4Ig on exptl. anti-glomerular basement membrane (GBM) autoimmune **glomerulonephritis** in Wistar-Kyoto rats induced by immunization with bovine GBM. The disease is characterized by development of antibody to the α3 chain of type IV collagen (Goodpasture's antigen), deposition of rat IgG in GBM, infiltration of the kidney by T cells and macrophages, severe crescent formation and renal failure leading to death in 5-6 wk. Animals injected with human CTLA4Ig from day 0 to day 14 or to day 35 had reduced disease severity. Beneficial effects were observed even when injections were begun after the onset of **glomerulonephritis** on day 14. However, the rats developed antibody to the human CTLA4Ig, associated with reduction in levels of circulating CTLA4Ig. The results provide evidence for CD28/CTLA-4 signaling in rat autoimmune **glomerulonephritis**, and suggest that more effective inhibition of B7-dependent T cell activation, such as might be achieved with homologous CTLA4Ig, could be useful in the treatment of autoimmune diseases.

L13 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:492997 HCAPLUS
DOCUMENT NUMBER: 119:92997
TITLE: Hyaluronate is a component of crescents in rat autoimmune **glomerulonephritis**
AUTHOR(S): **Nishikawa, Kazuhiro**; Andres, Giuseppe; Bhan, Atul K.; McCluskey, Robert T.; Collins, A. Bernard; Stow, Jennifer L.; Stamenkovic, Ivan
CORPORATE SOURCE: Dep. Pathol., Massachusetts Gen. Hosp., Boston, MA, USA
SOURCE: Laboratory Investigation (1993), 68(2), 146-53
CODEN: LAINAW; ISSN: 0023-6837
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Crescent formation in rapidly progressing kidney **glomerulonephritis** is generally associated with a poor prognosis. The crescents are formed by accumulation of monocyte/macrophages and blood plasma proteins in Bowman space, by proliferation of parietal epithelial cells and fibroblasts, and by deposition of the extracellular matrix. Interactions of components of the extracellular matrix with surface receptors of inflammatory cells may be important in the crescent formation. One such receptor is the glycoprotein CD44 whose main ligand is hyaluronic acid. Hyaluronate may be a component of crescents in a model of autoimmune antiglomerular basement membrane nephritis in rats. Rats were immunized with bovine glomerular basement membrane to induce severe crescentic **glomerulonephritis**. Sections of the renal tissue were studied with a soluble CD44-human Ig fusion protein and a hyaluronic acid-binding protein to detect hyaluronate. Both probes were detected by immunofluorescence techniques. The specificity of the reactions was established by selective enzymic digestions. Marked accumulations of hyaluronate were found in developing and sclerosing crescents, in association with local infiltration of T lymphocytes and monocyte/macrophages, cells known to express CD44. Lesser amts. of hyaluronate were found in periglomerular infiltrates. Hyaluronate is an abundant extracellular component of crescents and may play a critical role in their formation by influencing the migration and activation of CD44+ lymphocytes, monocyte/macrophages, fibroblasts, and epithelial cells.

L13 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1993:122871 HCAPLUS
DOCUMENT NUMBER: 118:122871

TITLE: Antibodies to intercellular adhesion molecule 1/lymphocyte function-associated antigen 1 prevent crescent formation in rat autoimmune **glomerulonephritis**

AUTHOR(S): **Nishikawa, Kazuhiro**; Guō, Ya Jun; Miyasaka, Masayuki; Tamatani, Takuya; Collins, A. Bernard; Sy, Man Sun; McCluskey, Robert T.; Andres, Giuseppe

CORPORATE SOURCE: Dep. Pathol., Massachusetts Gen. Hosp., Boston, MA, 02129, USA

SOURCE: Journal of Experimental Medicine (1993), 177(3), 667-77
CODEN: JEMEAV; ISSN: 0022-1007

DOCUMENT TYPE: Journal

LANGUAGE: English

AB In patients with **glomerulonephritis** widespread crescents are associated with a poor prognosis. Crescent formation appears to depend on the migration of mononuclear cells into Bowman's space, and therefore the interaction between leukocytes and glomerular endothelium may be a critical event in the genesis of crescents. The present study was performed to determine the effects of mouse monoclonal antibodies to the adhesion mols. ICAM-1 and LFA-1 antigen in a model of crescentic **glomerulonephritis** in Wistar-Kyoto rats, induced by immunization with bovine glomerular basement membrane (GBM). By 10-14 d after immunization, the rats had developed circulating anti-GBM antibodies, reactive with the α3 chain of type IV collagen (the Goodpasture antigen), accompanied by proteinuria, accumulation of rat IgG in the GBM, increased expression of ICAM-1 by glomerular endothelial cells, infiltration of glomerular tufts with LFA-1+ T cells and monocyte/macrophages, and early crescents. At 5 wk all rats had diffuse fibrocellular crescents, glomerular scleroiss, and tubulointerstitial damage. All rats developed severe renal insufficiency and died by 5 or 6 wk. The administration of monoclonal antibodies to rat ICAM-1 and LFA-1 markedly decreased the severity of the renal disease. In a group of rats injected 3 times/wk with the monoclonal antibodies, from 2 d before immunization with GBM to day 14, glomerular abnormalities and proteinuria were virtually absent at day 14; even at 5 wk glomerular disease was quite mild, with only slight crescent formation and with only a mild decrease in renal function. When treatment was continued until 5 wk, the beneficial effects were even more marked, with virtual absence of crescents and with preservation of normal renal function. In a group of rats in which treatment was initiated on day 14, shortly after the appearance of glomerular abnormalities, progression of the disease was appreciably retarded, and the decrease in renal function was inhibited. The kidneys of rats treated from days -2 to 14 with antibodies to ICAM-1 and LFA-1 showed bright linear staining for rat IgG along the GBm, which did not differ in intensity from that seen in untreated rats. Furthermore, the titers of anti-GBM antibodies at 2 wk in treated rats were not lower than that seen in most of the untreated rats. There was, however, moderate reduction of anti-GBM antibodies at 5 wk in the treated rats. In addition, in rats in which treatment was started after onset of the disease, the titers of anti-GBM antibodies did not decrease, although the progression of disease was inhibited. Thus, the preventive or therapeutic effects of antibodies to ICAM-1 and LFA-1 in rat anti-GBM **glomerulonephritis** probably resulted mainly from interference with interaction between leukocytes and activated glomerular endothelium, although reduction in the autoimmune response may have contributed to the beneficial effects. The results raise the possibility that similar treatment might be used to limit the progression of glomerular damage in human crescentic **glomerulonephritis**.

L13 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:580720 HCAPLUS
DOCUMENT NUMBER: 115:180720
TITLE: Involvement of thromboxane A2, leukotrienes and free radicals in puromycin nephrosis in rats
AUTHOR(S): **Shibouta, Yumiko**; Terashita, Zenichi; Imura, Yoshimi; Shino, Akio; Kawamura, Masaki; Ohtsuki, Kayoko; Ohkawa, Shigenori; **Nishikawa, Kohei**; Fujiwara, Yoshihiro
CORPORATE SOURCE: Res. Dev. Div., Takeda Chem. Ind., Ltd., Osaka, 532, Japan
SOURCE: Kidney International (1991), 39(5), 920-9
CODEN: KDYIA5; ISSN: 0085-2538
DOCUMENT TYPE: Journal
LANGUAGE: English
AB TXA2, leukotrienes (LTs) and free radicals are considered to be possible mediators in the induction of glomerular injury and proteinuria. This study examined the involvement of these three mediators and the protective effect of simultaneous inhibition of all three in puromycin aminonucleoside (PAN) nephrosis in rats. A single i.p. injection of PAN (100 mg/kg) induced massive proteinuria and enhanced production of TXA2 and LTs from arachidonic acid in renal cortical slices and renal glomeruli, and increased malondialdehyde levels in plasma, urine and renal cortex. Oral administration of CV-6504(HCl) (3 to 20 mg/kglday, for 1 to 2 wk), a novel treble inhibitor of TXA2 synthetase, 5-lipoxygenase and lipid peroxidn., dose-dependently attenuated PAN-induced proteinuria and the increased in these three mediators. Any single specific inhibitor (CV-4151, a TXA2 synthetase inhibitor; AA-861, a 5-lipoxygenase inhibitor; or CV-3611, a radical scavenger) or a combination of two inhibitors showed no or only a slight antiproteinuric effect, but the combination of all three inhibitors reduced PAN-induced proteinuria. These results suggest that, these three mediators may be involved in the pathogenesis of PAN nephrosis and that CV-6504(HCl), which can simultaneously inhibit all three, may be a useful therapeutic agent for nephrosis.

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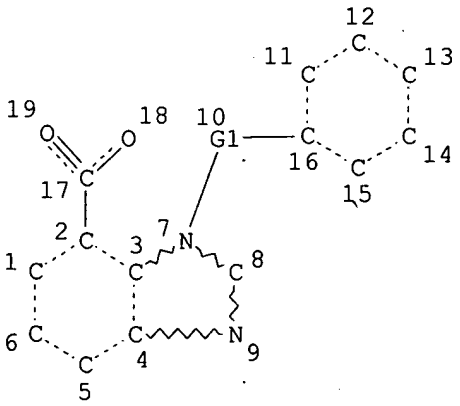
L5 STR



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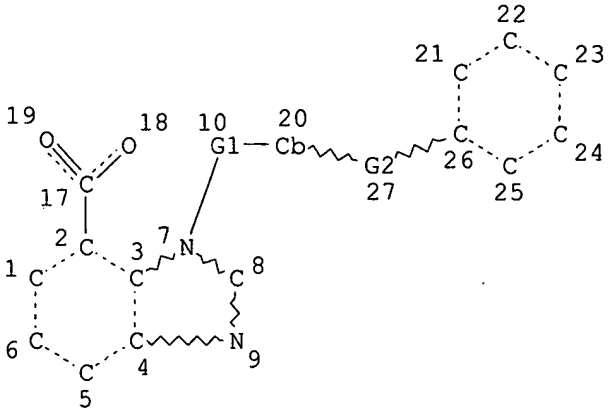
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L6 (595) SEA FILE=REGISTRY SSS FUL L5
L7 STR



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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
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STEREO ATTRIBUTES: NONE
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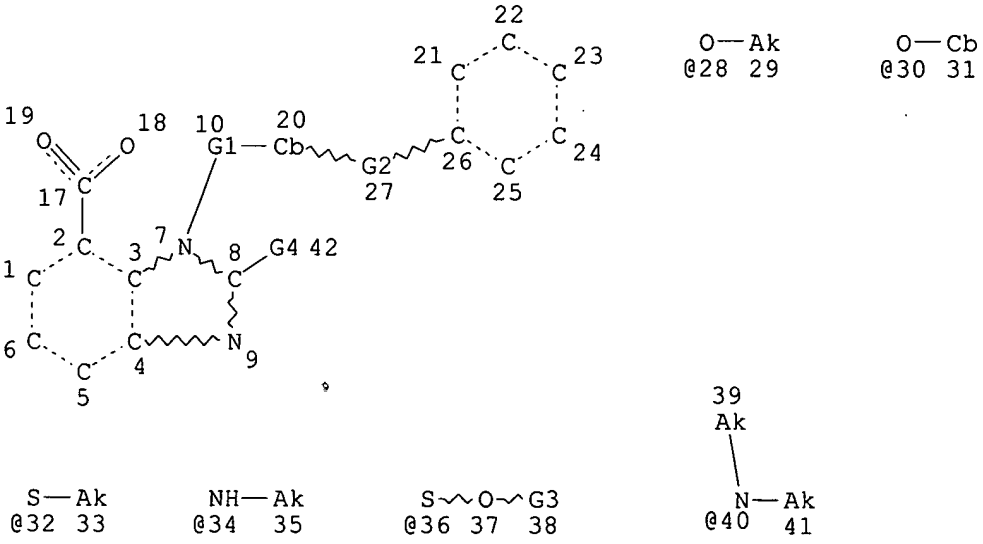
L14 STR



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REP G2=(0-2) A

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NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 36

STEREO ATTRIBUTES: NONE
L16 370 SEA FILE=REGISTRY SUB=L8 SSS FUL L14
L17 15 SEA FILE=HCAPLUS L16 AND GLOMERULONEPHRITIS

=> d ibib abs hitstr l17 1-15

L17 ANSWER 1 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:371095 HCAPLUS
DOCUMENT NUMBER: 142:423895
TITLE: Methods for controlling mast cell-derived renin and uses in treating conditions with abnormal renin levels
INVENTOR(S): Silver, Randi B.; Levi, Roberto
PATENT ASSIGNEE(S): Cornell Research Foundation, Inc., USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005037317	A2	20050428	WO 2004-US33755	20041013

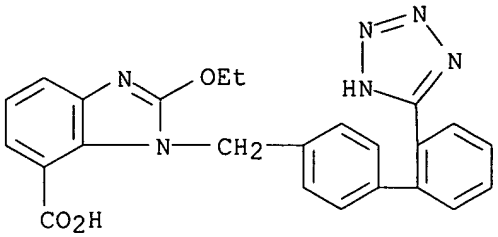
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2003-512142P P 20031017

AB The invention relates to the discovery that renin is present in mast cells and can act in a localized manner to initiate and/or exacerbate a number of conditions. Thus, the invention provides methods for treating cardiac, vascular, lung, liver, cervical, intestinal, muscle, pancreatic, brain, kidney, skin and other conditions that involve inhibiting the synthesis and/or release of renin from mast cells and/or inhibiting the activity of renin after release from mast cells. The methods of the invention can also involve inhibiting elements of the local renin-angiotensin system (e.g. inhibiting ACE and angiotensin II receptors), thereby inhibiting angiotensin II produced locally from mast-cell-derived renin.

IT **139481-59-7**, Candesartan
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for controlling mast cell-derived renin and uses in treating conditions with abnormal renin levels)

RN 139481-59-7 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 2 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:24246 HCAPLUS
DOCUMENT NUMBER: 142:329391
TITLE: Pirfenidone and candesartan ameliorate morphological damage in mild chronic anti-GBM nephritis in rats
AUTHOR(S): Leh, Sabine; Vaagnes, Oyvind; Margolin, Solomon B.; Iversen, Bjarne M.; Forslund, Terje
CORPORATE SOURCE: Renal Research Group, Institute of Internal Medicine, Univ. Bergen, Bergen, Norway
SOURCE: Nephrology, Dialysis, Transplantation (2005), 20(1), 71-82
CODEN: NDTREA; ISSN: 0931-0509
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: The antifibrotic substance pirfenidone and the angiotensin II type I receptor antagonist candesartan cilexetil, given alone and in combination, were tested in rats with chronic anti-glomerular basement membrane **glomerulonephritis** (anti-GBM GN). Methods: Male Wistar rats with anti-GBM GN were treated for 8 wk with candesartan (4 mg/kg body weight/day), pirfenidone (500 mg/kg body weight/day) or a combination of both drugs. One GN group received no treatment and untreated non-GN-rats were used as controls. Blood pressure and urinary protein excretion were measured after 3 and 7 wk. Kidney histol. was complemented by ultrastructural investigation and by quantification of collagen Iα mRNA. Results: The percentage of glomeruli with adsorption droplets in podocytes correlated well with the amount of proteinuria ($r = 0.873$, $P<0.01$) and was significantly lowered in rats treated with candesartan (8.3 vs GN 24.6%), pirfenidone (9.8%) and combined treatment (2.6%, $P<0.05$ vs candesartan alone). A comparable lowering was seen for segmental sclerosis (GN 11%, candesartan 0.7%, $P<0.05$ vs GN, pirfenidone 1.8%, $P = 0.09$ vs GN, candesartan/pirfenidone 0.1%, $P>0.5$ vs candesartan alone). Cortical collagen Iα mRNA expression was significantly decreased in all treatment groups. Ultrastructural investigation showed an amelioration of basement membrane alterations and podocyte damage in the treatment groups. Candesartan caused significant blood pressure reduction and the effect was significantly enhanced by combination therapy after 3 wk. Rats treated with pirfenidone showed blood pressure values similar to control rats. Conclusion: Pirfenidone has a beneficial effect on morphol. changes in anti-GBM GN comparable with candesartan although with a trend to slightly better results with candesartan treatment. Moreover, our results suggest an additive effect of combination treatment.

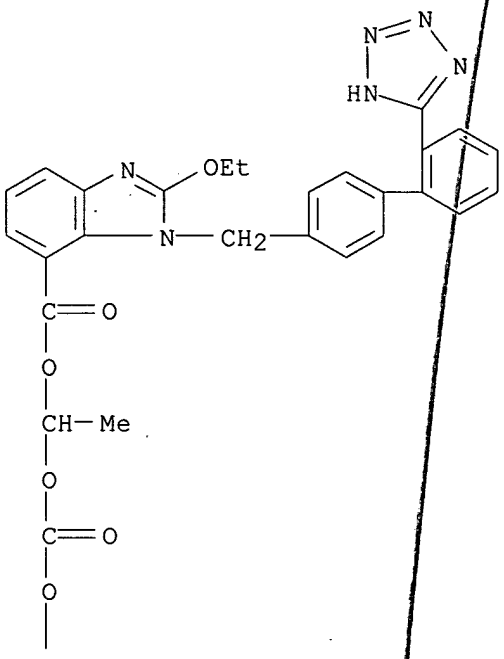
IT **145040-37-5**, Candesartan cilexetil

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(candesartan cilexetil alone or in combination with pirfenidone significantly reduced proteinuria, podocyte damage, tubular degeneration and collagen Iα expression in mild chronic anti-GBM **glomerulonephritis** rat model)

RN 145040-37-5 HCAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, 1-[[(cyclohexyloxy)carbonyl]oxy]ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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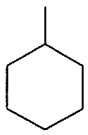

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:995983 HCAPLUS
DOCUMENT NUMBER: 141:388706
TITLE: Fortifier
INVENTOR(S): Kurumatani, Hajimu; Tamura, Mitsutaka
PATENT ASSIGNEE(S): Toray Industries Inc., Japan
SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004098611	A1	20041118	WO 2004-JP6412	20040506

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RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

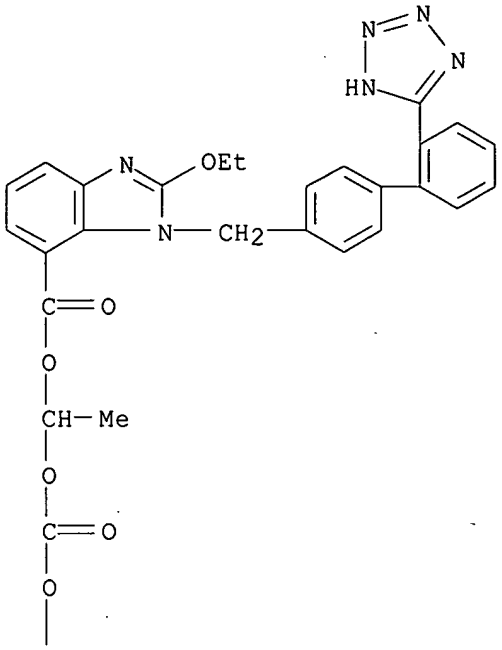
PRIORITY APPLN. INFO.: JP 2003-131664 A 20030509
OTHER SOURCE(S): MARPAT 141:388706

AB A fortifier capable of fortifying the therapeutic or preventive effects of renin-angiotensin inhibitor, such as Candesartan cilexetil, on kidney diseases. This fortifier comprises a specified prostaglandin I derivative, such as Beraprost Sodium, as an active ingredient.

IT **145040-37-5**, Candesartan cilexetil **147403-03-0**, TAK-536
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(renin-angiotensin and ACE inhibitors and PGI derivs. for treatment of kidney diseases)

RN 145040-37-5 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, 1-[[(cyclohexyloxy)carbonyl]oxy]ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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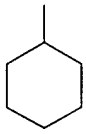
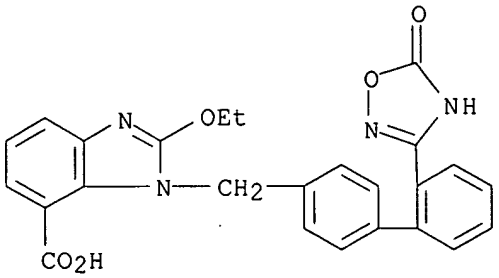


RN 147403-03-0 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)[1,1'-biphenyl]-4-yl]methyl]-2-ethoxy- (9CI) (CA INDEX NAME)



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L17 ANSWER 4 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:351638 HCAPLUS
DOCUMENT NUMBER: 140:350628
TITLE: Prophylactic and therapeutic agents for treatment of fibrosis-associated chronic kidney disorders
INVENTOR(S): Nakagawa, Tsutomu; Nagamine, Jun
PATENT ASSIGNEE(S): Sumitomo Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 26 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004131444	A2	20040430	JP 2002-298927	20021011
PRIORITY APPLN. INFO.:			JP 2002-298927	20021011
OTHER SOURCE(S):	MARPAT 140:350628			

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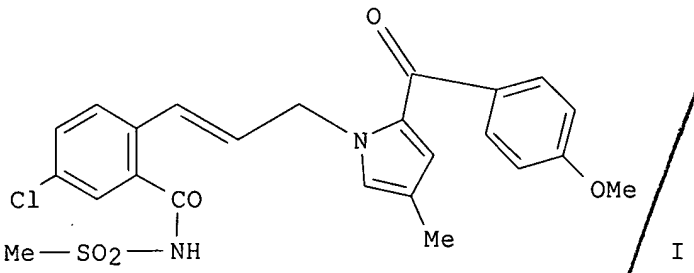
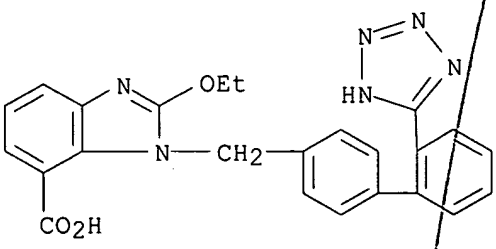


I

AB Title agents, which are used in combination with kidney-protecting pharmaceuticals, contain fibrosis inhibitors as active ingredients, or vice-versa. Thus, pyrrole derivative I (TGF-β inhibitor) and losartan showed synergistic efficacy in diabetic nephropathy in C57BL/KsJ-db/db mice.

IT **139481-59-7**, Candesartan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synergistic drugs containing kidney-protecting agents and fibrosis inhibitors for treatment of fibrosis-associated chronic kidney disorders)

RN 139481-59-7 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



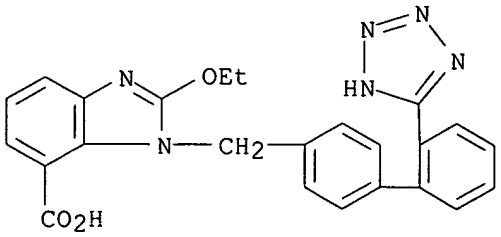
L17 ANSWER 5 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:203626 HCAPLUS
DOCUMENT NUMBER: 140:247061
TITLE: Conjoint administration of morphogens and ACE inhibitors in treatment of chronic renal failure
INVENTOR(S): Charette, Marc F.; Hruska, Keith A.; McCartney, John
PATENT ASSIGNEE(S): Curis, Inc., USA; Washington University in St. Louis
SOURCE: PCT Int. Appl., 295 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004019876	A2	20040311	WO 2003-US26923		20030828
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2497048	AA	20040311	CA 2003-2497048		20030828
PRIORITY APPLN. INFO.:			US 2002-406431P	P	20020828
			WO 2003-US26923	W	20030828

AB The present invention provides reagents and methods for the treatment, and pharmaceuticals for use in the prevention and/or treatment, of chronic renal failure and other renal disorders in subjects (particularly mammalian subjects) renal replacement therapy. The methods involve the conjoint administration of ACE (Angiotensin-Converting Enzyme) inhibitors or Angiotensin II Receptor Antagonists (AIIRAs) with one or more OP/BMP family of proteins (morphogens, or inducers of morphogens, or agonists of the corresponding morphogen receptors, etc.). The invention also provides methods for implantation of renal cells induced with the conjoint administration of ACE inhibitors or AIIRAs with those morphogens.

IT **139481-59-7**, Candesartan
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conjoint administration of morphogens and ACE inhibitors in treatment of chronic renal failure)

RN 139481-59-7 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



L17 ANSWER 6 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:842021 HCAPLUS
DOCUMENT NUMBER: 140:314722
TITLE: Use of candesartan cilexetil decreases proteinuria in renal transplant patients with chronic allograft dysfunction
AUTHOR(S): Omoto, Kazuya; Tanabe, Kazunari; Tokumoto, Tadahiko; Shimmura, Hiroaki; Ishida, Hideki; Toma, Hiroshi
CORPORATE SOURCE: Department of Urology, Kidney Center, Tokyo Women's Medical University, Tokyo, Japan
SOURCE: Transplantation (2003), 76(8), 1170-1174
CODEN: TRPLAU; ISSN: 0041-1337
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Posttransplant proteinuria and hypertension are difficult to treat after renal transplantation. Therefore, we examined whether candesartan cilexetil is effective in reducing urinary protein excretion or in controlling hypertension in patients with renal allograft dysfunction. Sixty-two renal transplant recipients with proteinuria were enrolled in this study. They underwent kidney transplantation under cyclosporine or tacrolimus immunosuppression between Feb. 1983 and Dec. 1998. Causes of proteinuria were chronic rejection in 28, **glomerulonephritis** in 16, cyclosporine or tacrolimus nephrotoxicity in 9, and unknown in 9 recipients. The dose of candesartan cilexetil ranged from 4 to 12 mg/day. Eleven patients with proteinuria who had not been treated with candesartan cilexetil constituted a matched control population. Hypertension was well controlled by administration of candesartan cilexetil. Both systolic blood pressure and diastolic blood pressure significantly decreased from 141.7±14.8 mm Hg to 118.7±11.9 mm Hg and 121.2±11.6 mm Hg, and from 89.0±13.0 mm Hg to 72.0±10.4 mm Hg and 74.9±9.4 mm Hg, at 2 mo and 1 yr after administration, resp. Urinary protein excretion was reduced from 0.93±1.2 g/day to 0.34±0.7 g/day and 0.43±1.2 g/day at 2 mo and 1 yr after administration, resp. The levels of creatinine clearance were 55.7±28.9 mL/min before treatment, 50.9±24.8 mL/min at 2 mo, and 52.6±24.8 mL/min at 1 yr after treatment, resp. There was no clin. significant difference between them. Regarding the calcineurin inhibitor levels, there was no significant difference between the levels before and 1 yr after treatment. There was a significant difference in all examns. (systolic blood pressure, diastolic blood pressure, proteinuria, and renal function) between the patients with and without candesartan at 1 yr after treatment. No significant adverse effects occurred. Candesartan cilexetil can effectively control hypertension and proteinuria without deterioration in renal allograft function. These data suggest that treatment with candesartan cilexetil may be useful for maintaining long-term renal allograft function.

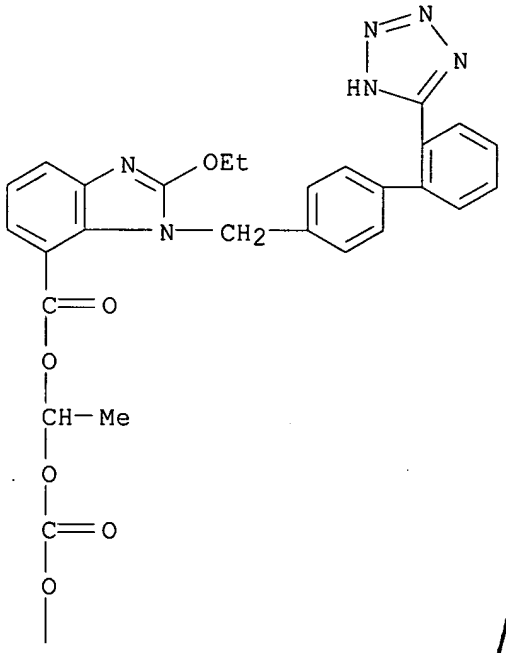
IT **145040-37-5**, Candesartan cilexetil

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(candesartan cilexetil effect on proteinuria and hypertension in renal transplant patients with chronic allograft dysfunction)

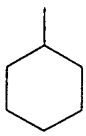
RN 145040-37-5 HCAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, 1-[[(cyclohexyloxy)carbonyl]oxy]ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 7 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:96708 HCAPLUS

DOCUMENT NUMBER: 138:163223

TITLE: Antiproteinuric effect of candesartan cilexetil in patients with chronic **glomerulonephritis**

AUTHOR(S): Kurokawa, Kiyoshi; Abe, Keishi; Saruta, Takao; Arakawa, Masaaki; Kikkawa, Ryuichi; Ueda, Naohiko; Onoyama, Kaoru; Tomita, Kimio; Ogawa, Nobuya

CORPORATE SOURCE: Department of Internal Medicine VII, School of

Medicine, Tokai University, Isehara, Kanagawa, Japan
SOURCE: JRAAS (2002), 3(3), 167-175
CODEN: JRAAAG; ISSN: 1470-3203
PUBLISHER: JRAAS Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

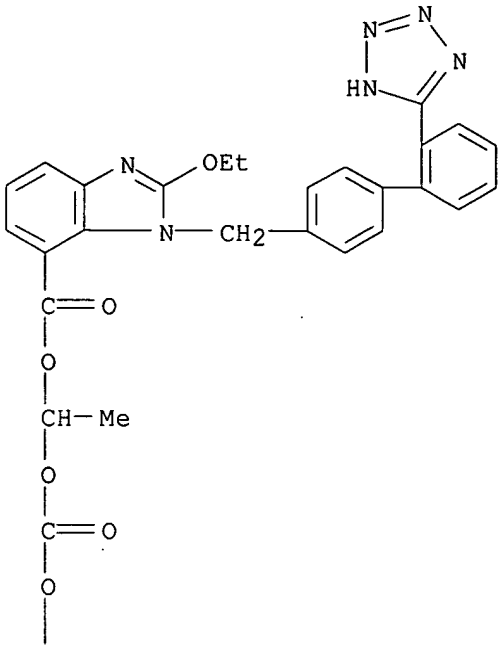
AB A prospective, randomized, double-blind, parallel-group, dose-response trial was conducted to investigate the antiproteinuric effect of candesartan cilexetil, the angiotensin II type 1 receptor blocker, in patients with chronic **glomerulonephritis**. Patients (n = 280) were treated for 12 wk with candesartan cilexetil 2, 4, or 8 mg given orally once-daily (o.d.). The improvement in urinary protein excretion observed at the end of the treatment period was 15.9% in the 2 mg group, 25.6% in the 4 mg group, and 34.6% in the 8 mg group, resp., showing a clear dose-response (2 mg < 4 mg < 8 mg; p = 0.003). The mean reduction in urinary protein excretion was 11.3% in the 2 mg group, 26.3% in the 4 mg group, and 26.0% in the 8 mg group, showing a dose-response pattern, in that the effect of 4 mg and 8 mg was greater than that of 2 mg (2 mg < 4 mg ≈ 8 mg; p = 0.010). As the observed reduction in urinary protein excretion failed to correlate with changes in mean blood pressure, it could not be attributed to the antihypertensive effect of the study drug alone. This suggests that candesartan cilexetil, 4 - 8 mg o.d., has antiproteinuric effects in patients with chronic **glomerulonephritis**.

IT **145040-37-5**, Candesartan cilexetil
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antiproteinuric effect of candesartan cilexetil in patients with chronic **glomerulonephritis**)

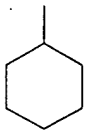
RN 145040-37-5 HCAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, 1-[[(cyclohexyloxy)carbonyl]oxy]ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

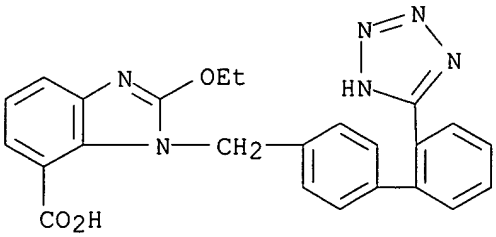
L17 ANSWER 8 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:463733 HCAPLUS
DOCUMENT NUMBER: 137:277157
TITLE: Fractalkine expression and the recruitment of CX3CR1+ cells in the prolonged mesangial proliferative **glomerulonephritis**
AUTHOR(S): Ito, Yumi; Kawachi, Hiroshi; Morioka, Yoshio; Nakatsue, Takeshi; Koike, Hiroko; Ikezumi, Yohei; Oyanagi, Akihisa; Natori, Yasuhiro; Natori, Yumiko; Nakamura, Takamichi; Gejyo, Fumitake; Shimizu, Fujio
CORPORATE SOURCE: Department of Cell Biology, Niigata University Graduate School of Medical and Dental Sciences, Niigata, Japan
SOURCE: Kidney International (2002), 61(6), 2044-2057
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We established the reversible and the prolonged models of mesangial proliferative **glomerulonephritis** (GN) with anti-Thy 1 antibody 1-22-3. However, the essential factors leading to the prolonged glomerular alterations were not identified. The expressions of several chemokines and cytokines were compared in the reversible and the prolonged models. Expression of fractalkine and the number of the fractalkine receptor CX3CR1-pos. cells in the glomeruli in the prolonged model were significantly higher than those in the reversible model. Then, the localization of fractalkine and the characteristics of CX3CR1- cells were analyzed in glomeruli. To elucidate the significance of the fractalkine expression, the authors analyzed the expression in the model treated with angiotensin II receptor antagonist, candesartan. Immunostaining of fractalkine was detected on endothelial cells on the fifth day, and fractalkine staining also was detected in the mesangial area on day 14. Major parts of the CX3CR1+ cells in the glomeruli were macrophages, especially ED3+ cells. Candesartan treatment ameliorated the glomerular morphol. findings at six weeks after disease induction. Although the treatment did not ameliorate the morphol. finding at two weeks, decreased expression of fractalkine and CX3CR1+ were already detected at two weeks in rats treated with candesartan. Fractalkine expression and the recruitment of CX3CR1+ cells in glomeruli might play an important role in the development of the prolonged disease. These expressions could be predictors of the prolonged disease of the mesangial proliferative **glomerulonephritis**.

IT **139481-59-7**, Candesartan
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(candesartan decreased CX3CR1 expression and increased MCP-1 in glomeruli cells in prolonged mesangial proliferative **glomerulonephritis**)

RN 139481-59-7 HCAPLUS

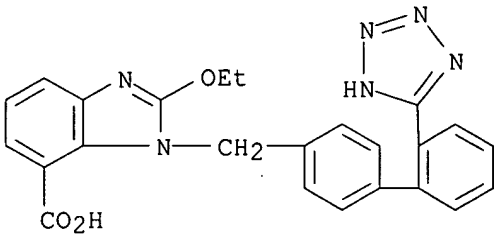
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 9 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:411473 HCAPLUS
DOCUMENT NUMBER: 137:288766
TITLE: Augmentation of anti-proteinuric effect by combined therapy with angiotensin II receptor blocker plus calcium channel blocker in a hypertensive patient with IgA **glomerulonephritis**
AUTHOR(S): Kuriyama, S.; Tomonari, H.; Abe, A.; Kunieda, T.; Hosoya, T.
CORPORATE SOURCE: Div. Nephrol., Saiseikai Cent. Hosp., Tokyo, Japan
SOURCE: Journal of Human Hypertension (2002), 16(5), 371-373
CODEN: JHHYEN; ISSN: 0950-9240
PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal
LANGUAGE: English
AB The efficacy of combined therapy with calcium channel blocker and angiotensin II receptor blocker (ARB) was tested in a hypertensive patient with IgA nephropathy. The addition of the ARB candesartan to the long-acting CCB amlodipine significantly reduced the urinary protein excretion, without any change in blood pressure and serum creatinine concentration CCB was withdrawn to confirm the additive antiproteinuric effect of the ARB alone. The withdrawal resulted in a partial return of protein excretion, suggesting that the combination of an ARB with a CCB has a marked additive effect on protein excretion in patients with progressive renal disease.
IT **139481-59-7**, Candesartan
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiotensin II receptor blocker plus calcium channel blocker augmentation of antiproteinuric effect with combined therapy in hypertensive patient with IgA **glomerulonephritis**)
RN 139481-59-7 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 10 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:53388 HCAPLUS
DOCUMENT NUMBER: 132:98146
TITLE: Pharmaceutical composition containing, in combination, an antagonist of the angiotensin II AT1 receptors and indomethacin for treatment of chronic **glomerulonephritis**
INVENTOR(S): Brouard, Remi; Remuzzi, Giuseppe
PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002556	A1	20000120	WO 1999-FR1650	19990708

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,

TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

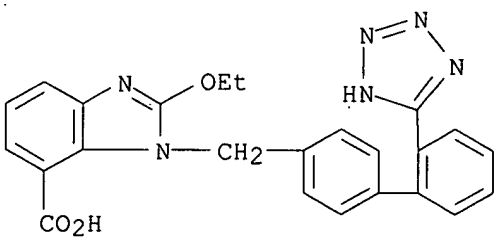
FR 2780890	A1	20000114	FR 1998-8976	19980710
FR 2780890	B3	20000901		
AU 9946252	A1	20000201	AU 1999-46252	19990708
EP 1115399	A1	20010718	EP 1999-929432	19990708
EP 1115399	B1	20050302		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 289811	E	20050315	AT 1999-929432	19990708

PRIORITY APPLN. INFO.: FR 1998-8976 A 19980710
WO 1999-FR1650 W 19990708

AB A pharmaceutical composition contains, in combination, indomethacin and an antagonist of the angiotensin II AT1 receptors, in particular irbesartan, for treatment of chronic **glomerulonephritis**. Patients having chronic **glomerulonephritis** were given 100 irbesartan for 28 days then combined it with 75 mg indomethacin for 3 more days. The total protein content of the urine was 0.57 as compared with 2.48 g/24 h for the controls. A capsule contained indomethacin 50.00, irbesartan 150.00, lactose monohydrate 252.35, maize starch 57.77, colloidal silica 2.13, magnesium stearate 4.25, talc 8.50 mg.

IT **139481-59-7**, Candesartan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical composition containing, in combination, antagonist of angiotensin II AT1 receptors and indomethacin for treatment of chronic **glomerulonephritis**)

RN 139481-59-7 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 11 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:180467 HCAPLUS
DOCUMENT NUMBER: 131:27684
TITLE: Blocking angiotensin II ameliorates proteinuria and glomerular lesions in progressive mesangioproliferative **glomerulonephritis**
AUTHOR(S): Nakamura, Takamichi; Obata, Jun-Ei; Kimura, Hideaki; Ohno, Shinichi; Yoshida, Yoji; Kawachi, Hiroshi; Shimizu, Fujio
CORPORATE SOURCE: Division of Blood Transfusion, Department of Internal

Medicine, Department of Anatomy, Department of Pathology, Yamanashi Medical University, Yamanashi, Japan

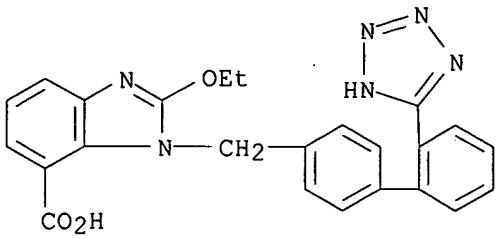
SOURCE: Kidney International (1999), 55(3), 877-889
CODEN: KDYIA5; ISSN: 0085-2538
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The renin-angiotensin system is thought to be involved in the progression of **glomerulonephritis** (GN) into end-stage renal failure (ESRF) because of the observed renoprotective effects of angiotensin-converting enzyme inhibitors (ACEIs). However, ACEIs have pharmacol. effects other than ACE inhibition that may help lower blood pressure and preserve glomerular structure. We previously reported a new animal model of progressive glomerulosclerosis induced by a single i.v. injection of an anti-Thy-1 monoclonal antibody, MoAb 1-22-3, in uninephrectomized rats. Using this new model of progressive GN, we examined the hypothesis that ACEIs prevent the progression to ESRF by modulating the effects of angiotensin II (Ang II) on the production of transforming growth factor-β (TGF-β) and extracellular matrix components. We studied the effect of an ACEI (cilazapril) and an Ang II type 1 receptor antagonist (candesartan) on the clin. features and morphol. lesions in the rat model previously reported. After 10 wk of treatment with equihypotensive doses of cilazapril, cilazapril plus Hoe 140 (a bradykinin receptor B2 antagonist), candesartan, and hydralazine, we examined systolic blood pressure, urinary protein excretion, creatinine clearance, the glomerulosclerosis index, and the tubulointerstitial lesion index. We performed a semiquant. evaluation of glomerular immunostaining for TGF-β and collagen types I and III by immunofluorescence study and of these cortical mRNA levels by Northern blot anal. Untreated rats developed massive proteinuria, renal dysfunction, and severe glomerular and tubulointerstitial injury, whereas uninephrectomized control rats did not. There was a significant increase in the levels of glomerular protein and cortical mRNA for TGF-β and collagen types I and III in untreated rats. Cilazapril and candesartan prevented massive proteinuria, increased creatinine clearance, and ameliorated glomerular and tubulointerstitial injury. These drugs also reduced levels of glomerular protein and cortical mRNA for TGF-β and collagen types I and III. Hoe 140 failed to blunt the renoprotective effect of cilazapril. Hydralazine did not exhibit a renoprotective effect. These results indicate that ACEIs prevent the progression to ESRF by modulating the effects of Ang II via Ang II type 1 receptor on the production of TGF-β and collagen types I and III, as well as on intrarenal hemodynamics, but not by either increasing bradykinin activity or reducing blood pressure in this rat model of mesangial proliferative GN.

IT **139481-59-7**, Candesartan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(blocking angiotensin II ameliorates proteinuria and glomerular lesions in progressive mesangioproliferative **glomerulonephritis**)

RN 139481-59-7 HCAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



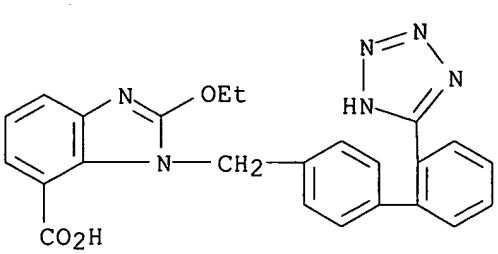
REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 12 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:118005 HCAPLUS
DOCUMENT NUMBER: 130:246685
TITLE: Effects of candesartan on the proteinuria of chronic **glomerulonephritis**
AUTHOR(S): Kurokawa, Kiyoshi
CORPORATE SOURCE: Tokai University, Boseidai Ishara, 259, Japan
SOURCE: Journal of Human Hypertension (1999), 13(Suppl. 1), S57-S60
CODEN: JHHYEN; ISSN: 0950-9240
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Angiotensin I-converting enzyme (ACE) inhibitors are commonly used for the treatment of hypertension, progressive chronic renal disease, diabetic nephropathy, and congestive heart failure. Because angiotensin II acts through membrane bound type 1 (AT1) and type 2 (AT2) receptors, ACE inhibitors and angiotensin II-receptor antagonists have distinct effects. ACE inhibitors inhibit production of angiotensin II thus suppressing the action of angiotensin II on both AT1 and AT2. In contrast, the effect of AT1-receptor antagonists is to selectively block the activation of the AT1 receptor. This AT1-receptor blockade leaves the AT2 receptors unopposed to elevated levels of endogenous angiotensin II. Thus, there may be an advantage of AT1-receptor blockade over ACE inhibition in the management of a variety of chronic vascular diseases, including chronic **glomerulonephritis** and other glomerular diseases. In a clin. trial candesartan, an AT1-receptor antagonist, effectively lowered urinary protein excretion in patients with chronic glomerular nephritis. Evidence indicates that functionally active AT1 receptors, as well as AT2 receptors, are present in both afferent and efferent arteriole of the glomerulus, and that angiotensin II induces afferent and efferent arteriolar dilatation via AT2 receptors.

IT **139481-59-7**, Candesartan
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of candesartan on the proteinuria of chronic **glomerulonephritis** in humans)

RN 139481-59-7 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



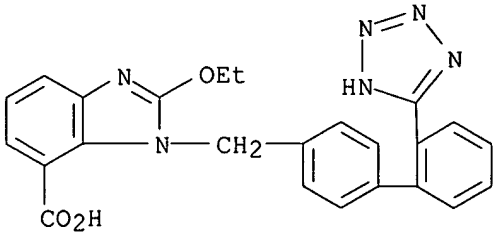
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 13 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:806365 HCAPLUS
DOCUMENT NUMBER: 128:110643
TITLE: Candesartan prevents the progression of mesangioproliferative nephritis in rats
AUTHOR(S): Nakamura, Takamichi; Obata, Jun-ei; Onizuka, Makoto; Kimura, Hideaki; Ohno, Shinichi; Yoshida, Yoji; Kawachi, Hiroshi; Zhimizu, Fujio
CORPORATE SOURCE: Departments of Internal Medicine, Anatomy, and Pathology, Yamanashi Medical University, Yamanashi, Japan
SOURCE: Kidney International, Supplement (1997), 63, S226-S228
CODEN: KISUDF; ISSN: 0098-6577
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We previously reported a new animal model of progressive **glomerulonephritis** induced by a single i.v. injection of the anti-Thy-1 monoclonal antibody MoAb 1-22-3 into uninephrectomized rats (Clin. Exp. Immunol. 102:181-185, 1995). We examined the effects of angiotensin II (Ang II) receptor antagonist (candesartan) on the clin. features and morphol. lesions of this new model. By 10 wk after induction of nephritis, untreated rats had developed hypertension, massive proteinuria, renal dysfunction, and severe glomerular injury, while uninephrectomized control rats had not. There was a significant increase in levels of glomerular protein and cortical mRNA for transforming growth factor-β (TGF-β) and type I and type III collagens in untreated nephritic rats. Ten week treatments with candesartan and hydralazine significantly reduced blood pressure (BP) to an equal extent. Candesartan, but not hydralazine, prevented proteinuria, normalized renal function, and ameliorated glomerular injury. Candesartan also reduced levels of glomerular protein and cortical mRNA for TGF-β and type I and type III collagens, while hydralazine did not. These findings suggest that candesartan prevents progression to end-stage renal failure by modulating the effects of Ang II at least in part on the production of TGF-β and type I and type III collagens, and not merely on systemic BP.

IT **139481-59-7**, Candesartan
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(candesartan prevents mesangioproliferative nephritis progression)

RN 139481-59-7 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 14 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:684304 HCAPLUS
DOCUMENT NUMBER: 127:351205
TITLE: Pharmaceutical compositions containing angiotensin II antagonists and additional agents for treatment of angiotensin II-mediated diseases
INVENTOR(S): Tamura, Norikazu; Sohda, Takashi; Ikeda, Hitoshi
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9737688	A2	19971016	WO 1997-JP1149	19970403
WO 9737688	A3	19980305		
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
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AU 9721780	A1	19971029	AU 1997-21780	19970403
AU 713277	B2	19991125		
CN 1215338	A	19990428	CN 1997-193515	19970403
EP 914158	A2	19990512	EP 1997-914592	19970403
EP 914158	B1	20020710		
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EP 1192951	A2	20020403	EP 2001-124024	19970403
EP 1192951	A3	20040421		
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RU 2188013	C2	20020827	RU 1998-119885	19970403
ES 2175385	T3	20021116	ES 1997-914592	19970403
PT 914158	T	20021129	PT 1997-914592	19970403
SK 283348	B6	20030603	SK 1998-1278	19970403

JP 09323940	A2	19971216	JP 1997-86484	19970404
US 6107323	A	20000822	US 1997-836784	19970516
NO 9804123	A	19980907	NO 1998-4123	19980907
US 6432996	B1	20020813	US 2000-551546	20000418
PRIORITY APPLN. INFO.:			JP 1996-83917	A 19960405
			EP 1997-914592	A3 19970403
			WO 1997-JP1149	W 19970403
			US 1997-836784	A3 19970516

OTHER SOURCE(S): MARPAT 127:351205

AB To provide a pharmaceutical composition which performs a remarkable effect with a relatively decreased dosage and with less side effects, a pharmaceutical composition was formulated by combination of an angiotensin II-mediated compound or a salt thereof with at least one species of a compound having the activity of increasing insulin sensitivity, a compound having the activity of improving postprandial hyperglycemia in diabetes mellitus, an indane derivative having the activity of inhibiting angiotensin-converting enzyme, a pyridine derivative having the activity of inhibiting HMG-Co A reductase or salts thereof. A capsule for treatment of arteriosclerosis was formulated containing 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]-methyl]-1H-benzimidazole-7-carboxylic acid 1, 5-[4-[-2-(5-ethyl-2-pyridyl)ethoxy]benzyl]-2,4-thiazolidinedione 30, lactose 69, microcryst. cellulose 70, and Mg stearate 10 mg.

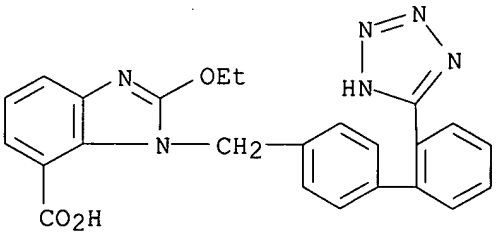
IT **139481-59-7 145040-37-5 147403-03-0**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical compns. containing angiotensin II antagonists and addnl. agents for treatment of angiotensin II-mediated diseases)

RN 139481-59-7 HCAPLUS

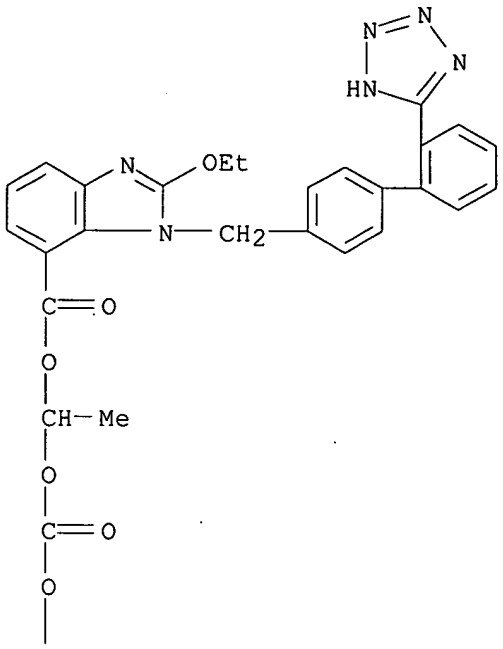
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]- (9CI) (CA INDEX NAME)



RN 145040-37-5 HCAPLUS

CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, 1-[[(cyclohexyloxy)carbonyl]oxy]ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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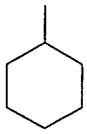
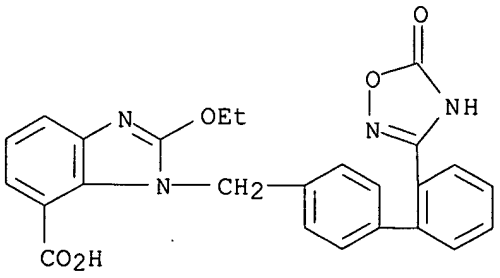


RN 147403-03-0 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)[1,1'-biphenyl]-4-yl]methyl]-2-ethoxy- (9CI) (CA INDEX NAME)



L17 ANSWER 15 OF 15 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:204117 HCAPLUS

DOCUMENT NUMBER: 126:195243
TITLE: Method for treating renal disease using an ACE inhibitor and an angiotensin II antagonist
INVENTOR(S): Remuzzi, Giuseppe; Eydelloth, Ronald S.; Owen, Roger A.; Shahinfar, Shahnaz
PATENT ASSIGNEE(S): Merck and Co., Inc., USA; Laboratoires Merck Sharp et Dohme-Chibret; Remuzzi, Giuseppe; Eydelloth, Ronald S.; Owen, Roger A.; Shahinfar, Shahnaz
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

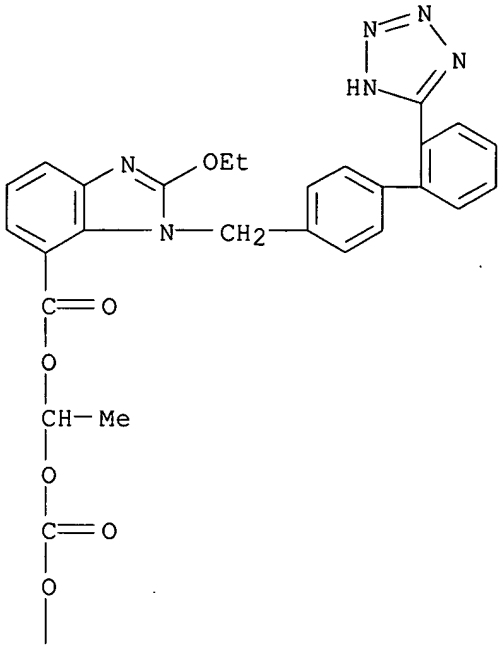
PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9702032	A1	19970123	WO 1996-US10942		19960626
W: AL, AM, AU, AZ, BB, BG, BR, BY, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
CA 2224451	AA	19970123	CA 1996-2224451		19960626
AU 9662916	A1	19970205	AU 1996-62916		19960626
AU 716519	B2	20000224			
EP 835106	A1	19980415	EP 1996-921794		19960626
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI					
JP 11508894	T2	19990803	JP 1996-505200		19960626
PRIORITY APPLN. INFO.:			US 1995-770P	P	19950630
			GB 1996-2854	A	19960213
			WO 1996-US10942	W	19960626

AB The present invention relates to a method of treating and/or preventing renal disease with the coadministration of an ACE inhibitor and an AII receptor antagonist. The present invention also relates to a method for protection of renal structure and/or renal function with the coadministration of an ACE inhibitor an an AII receptor antagonist. The combination is also useful in preventing renal injury and protecting glomerular structure. The effect of Lisinopril (ACE inhibitor) and Losartan (angiotensin II receptor antagonist) in animals with diabetic nephropathy is described.

IT **145040-37-5 147403-03-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ACE inhibitor and angiotensin II antagonist for treatment of renal disease)

RN 145040-37-5 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 2-ethoxy-1-[[2'-(1H-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-, 1-[[(cyclohexyloxy)carbonyl]oxy]ethyl ester (9CI) (CA INDEX NAME)

PAGE 1-A



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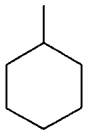
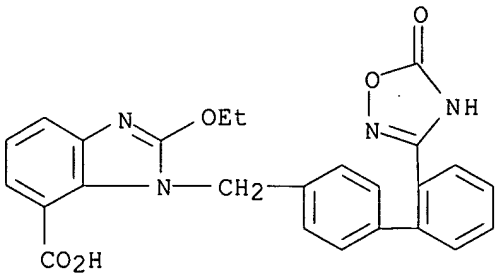


RN 147403-03-0 HCAPLUS
CN 1H-Benzimidazole-7-carboxylic acid, 1-[[2'-(2,5-dihydro-5-oxo-1,2,4-oxadiazol-3-yl)[1,1'-biphenyl]-4-yl]methyl]-2-ethoxy- (9CI) (CA INDEX NAME)



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